AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented): A compound comprising a polymeric diagnostic or therapeutic moiety (X) covalently conjugated to at least one PNA (P) and at least one targeting moiety (T) that is capable of binding to a cell surface molecule, wherein the PNA comprises a base sequence that is complementary to a target nucleic acid sequence, or pharmaceutically acceptable salts thereof, provided that the compound is represented by a formula

X-L1-P-L2-T

or pharmaceutically acceptable salts thereof, wherein L1 and L2 represent at least one linking moiety, provided that L1 is covalently bound to X and P and L2 is covalently bound to P and T.

2. (Canceled)

3. (Previously Presented): The compound of claim 1, wherein L1 and L2 can be the same or different, and are independently selected from the group consisting of -NH(O)C-CH2CH2-C(O)O- and -HN-CH2CH2-O-CH2CH2-O-CH2C(O)O, (Gly)4 and 4-amino butyric acid.

4. (Original): The compound of claim 1, comprising a diagnostic moiety.

5. (Withdrawn): The compound of claim 1, comprising a therapeutic moiety.

6. (Withdrawn): The compound of claim 1, wherein the diagnostic or therapeutic moiety comprises a linear oligomeric polychelant.

7. (Original): The compound of claim 1, wherein the diagnostic or therapeutic moiety comprises a branched oligomeric polychelant.

8. (Original): The compound of claim 1, wherein the diagnostic or therapeutic moiety comprises a dendrimer.

9. (Original): The compound of claim 8, wherein the dendrimer is selected from the group consisting of starburst dendrimers, cascade dendrimers controlled hyperbranched dendrimers and random hyperbranched dendrimers.

10. (Original): The compound of claim 8, wherein the dendrimer is a polyamidoamine (PAMAM) dendrimer, a polypropylamine (POPAM) dendrimer, a polyether (PE) dendrimer or a polyethyleneimine (PEI) dendrimer.

11. (Original): The compound of claim 1, wherein the diagnostic or therapeutic moiety comprises at least one biodegradation cleavage site.

12. (Original): The compound of claim 1, wherein the diagnostic or therapeutic moiety comprises a bridged dendrimeric or polymeric moiety.

13. (Original): The compound of claim 4, wherein the diagnostic moiety comprises a plurality of chelants optionally complexed to one or more diagnostic metal ions.

14. (Original): The compound of claim 13, wherein the diagnostic metal ion is a paramagnetic metal ion, a heavy metal ion or an ion of a radioactive metal isotope.

15. (Withdrawn): The compound of claim 14, wherein the paramagnetic metal ion is selected from the group consisting of Eu, Ho, Gd, Dy, Mn, Cr and Fe.

16. (Original): The compound of claim 14, wherein the paramagnetic metal ion is

selected from the group consisting of Gd(III), Mn(II) and Dy(III).

17. (Withdrawn): The compound of claim 14, wherein the heavy metal ion is selected from the group consisting of Hf, La, Yb, Dy and Gd.

18. (Withdrawn): The compound of claim 14, wherein the ion of radioactive metal isotopes is selected from the group consisting of 99mTc, 87Y, 67Ga, 68Ga, 64Cu, and 111In.

19. (Withdrawn): The compound of claim 4, wherein the diagnostic moiety comprises a diagnostic metal ion suitable for use in PET imaging.

20. (Withdrawn): The compound of claim 4, wherein the diagnostic moiety comprises a radioactive halogen.

21. (Withdrawn): The compound of claim 5, wherein the therapeutic moiety comprises a plurality of chelants optionally complexed to one or more therapeutic metal ions.

22. (Withdrawn): The compound of claim 21, wherein the therapeutic metal ion is an ion of a radioactive metal isotope.

23. (Withdrawn): The compound of claim 22, wherein the ion of a radioactive metal isotope is selected from the group consisting of 64Cu, 90Y, 105Rh, 111In, 117mSn, 149Pm, 153Sm, 161Tb, 166Dy, 166Ho, 175Yb, 177Lu, 186/188Re, 199Au, 47Sc, 67Cu, 67Ga, 212Pb, 68Ga, 212Bi, 210At, and 211At.

24. (Withdrawn): A compound of claim 1, wherein the polymeric diagnostic or therapeutic moiety comprises a plurality of NxSy chelants.

25. (Withdrawn): The compound of claim 24, wherein the NxSy chelants are N2S2 chelants, N3 chelants, N2S3 chelants, N2S4 chelants, N3S3 chelants, N4 chelants or NS3

chelants.

26. (Original): A compound of claim 1, wherein the polymeric diagnostic or therapeutic moiety comprises a plurality of linear, cyclic or branched polyamino-polycarboxylic acid chelants or their phosphorous oxyacid equivalents.

27. (Original): The compound of claim 26, wherein the linear, cyclic or branched polyamino-polycarboxylic acid chelants are selected from the group consisting of ethylenediamine-N,N,N',N'-tetraacetic acid (EDTA); N,N,N',N'',N''-diethylene-triaminepentaacetic acid (DTPA); 1,4,7,10-tetraazocyclododecane-N,N'N'',N'''-tetraacetic acid (DOTA); 1,4,7,10-tetraazo-cyclododecane-N,N'N''-triacetic acid (DO3A); 1-oxa-4,7,10-triazacyclododecane-N,N'N''-triacetic acid (OTTA); trans(1,2)-cyclohexanodiethylene-triamine-pentaacetic acid (CDTPA); 1-oxa-4,7,10-triazacyclododecantriaacetic acid (DOXA); 1,4,7-triazacyclononanetriacetic acid (NOTA); and 1,4,8,11-tetraazacyclotetradecanetetraacetic acid (TETA), and phosphorous oxyacid equivalents thereof.

28. (Original): The compound of claim 1, wherein the PNA comprises N-ethylaminoglycine backbone units, and the bases are covalently bound to the backbone units by methylene-carbonyl groups.

29. (Original): The compound of claim 1, wherein the PNA is about 8 to about 60 bases in length.

30. (Original): The compound of claim 1, wherein the target nucleic acid sequence comprises some or all of a consecutive sequence of bases in an RNA transcript.

31. (Original): The compound of claim 30, wherein the RNA transcript is

heteronuclear RNA or messenger RNA.

32. (Original): The compound of claim 30, wherein the RNA transcript is produced from an oncogene or proto-oncogene.

33. (Original): The compound of claim 32, wherein the oncogene or proto-oncogene is selected from the group consisting of K-RAS, c-MYB, BCR-ABL, p53, CCND1, HER2, MYC, c-FMS, c-KIT, c-MET, c-TRK, c-NEU, c-SRC, c-FES, c-ABL, c-FGR, c-YES, c-ERBA, c-EVI-1, c-GLI-1, c-MAF, c-LYL-1, c-ETS, c-FOS, c-JUN, c-MYB, b-MYB, N-MYC, L-MYC, c-REL, c-VAV, c-SKI, and c-SPI.

34. (Original): The compound of claim 1, wherein the targeting moiety is a protein, a glycoprotein, a peptide, a steroid, a carbohydrate, a lipid or a vitamin.

35. (Withdrawn): The compound of claim 34, wherein the protein-targeting moiety is selected from the group consisting of peptide hormones, antigens, antibodies, growth factors, cytokines, and peptide toxins.

36. (Withdrawn): The compound of claim 35, wherein the antibody-targeting moiety is selected from the group consisting of monoclonal antibodies, chimeric antibodies, single chain antibodies, humanized antibodies, and antibody fragments.

37. (Withdrawn): The compound of claim 1, wherein the targeting moiety is selected from the group consisting of folate, transferrin and fragments and homologs thereof, epidermal growth factor (EGF) and fragments and homologs thereof; platelet-derived growth factors and fragments and homologs thereof; urogastrone and analogs thereof; thyrotrypsin releasing hormone (TRH) and fragments and homologs thereof; nerve-growth factor (NGF) and fragments

and homologs thereof; an HIV viral antigen; α2-macroglobulin; thiodothyronine; thrombine; arachidonic acid; transforming growth factor-α (TGF-α) and fragments and homologs thereof; heregulins (HRGs) and fragments and homologs thereof; and alpha fetoprotein (AFP) and fragments and homologs thereof.

38. (Withdrawn): The compound of claim 1, wherein the targeting moiety is IGF1, ST, or fragments or homologs thereof.

39. (Withdrawn): The compound of claim 1, wherein the targeting moiety is the disulfide-bonded D-peptide Gly-Cys-Ser-Lys-Ala-Pro-Lys-Leu-Pro-Ala-Ala-Leu-Cys or the disulfide-bonded D-peptide Cys-Ser-Lys-Ala-Pro-Lys-Leu-Pro-Ala-Ala-Tyr-Cys.

40. (Withdrawn): The compound of claim 1, wherein the polymeric diagnostic agent comprises an ultrasound contrast agent.

41. (Original): A diagnostic imaging method, comprising:

(1) contacting cells of a subject that contain transcripts comprising a target nucleic acid sequence with a compound of claim 4, such that the compound binds to the cells via the targeting moiety and is internalized by the cell;

(2) allowing the PNA to bind to the target nucleic acid sequence and retain the compound inside the cell; and

(3) detecting the compound within the cells.

42. (Original): The method of claim 41, wherein the presence of the compound within the cells indicates a pathological state.

43. (Original): The method of claim 41, wherein the diagnostic moiety comprises a

dendrimer.

44. (Original): The method of claim 41, wherein the diagnostic moiety comprises a plurality of chelants optionally complexed to one or more diagnostic metal ions.

45. (Original): The method of claim 44, wherein the diagnostic metal ion is a paramagnetic metal ion, a heavy metal ion or an ion of a radioactive metal isotope.

46. (Withdrawn): The method of claim 41, wherein the diagnostic moiety comprises a diagnostic metal ion suitable for use in PET imaging.

47. (Withdrawn): The method of claim 41, wherein the diagnostic moiety comprises a radioactive halogen.

48. (Original): The method of claim 42, wherein the pathological state is cancer.

49. (Original): The method of claim 48, wherein the cancer is pancreatic or breast cancer.

50. (Original): The method of claim 41, wherein the target nucleic acid sequence comprises some or all of a consecutive sequence of bases in an RNA transcript.

51. (Original): The method of claim 41, wherein the RNA transcript is produced from an oncogene or proto-oncogene.

52. (Original): The method of claim 41, wherein the targeting moiety is a protein, a glycoprotein, a peptide, a steroid, a carbohydrate, a lipid or a vitamin.

53. (Withdrawn): The method of claim 41, wherein the targeting moiety is IGF1, ST, or fragments or homologs thereof.

54. (Previously Presented): The method of claim 41, wherein the compound is

detected within the cells by magnetic resonance imaging (MRI), scintigraphic imaging, X-ray, gamma camera imaging, ultrasound, or detection of fluorescent or visible light.

55. (Original): The method of claim 41, wherein the cells are contacted with the compound by an enteral or parenteral route of administration.

56. (Original): The method of claim 55, wherein the parenteral administration routes are selected from the group consisting of intravascular administration; peri- and intra-tissue injection; subcutaneous injection; subcutaneous deposition; subcutaneous infusion; and direct application to the tumor or to tissue surrounding a tumor.

57. (Withdrawn): A therapeutic method, comprising:

(1) contacting cells of a subject that contain transcripts comprising a target nucleic acid sequence indicative of a pathological state with a compound of claim 5, such that the compound binds to the cells via the targeting moiety and is internalized by the cell;

(2) allowing the PNA to bind to the target nucleic acid sequence and retain the compound inside the cell, wherein the presence of the compound within the cell inhibits cell growth or causes death of the cell.

58. (Withdrawn): The method of claim 57, wherein the therapeutic moiety comprises a dendrimer.

59. (Withdrawn): The method of claim 57, wherein the therapeutic moiety comprises a plurality of chelants optionally complexed to one or more therapeutic metal ions.

60. (Withdrawn): The method of claim 59, wherein the therapeutic metal ion is an ion of a radioactive metal isotope.

61. (Withdrawn): The method of claim 57, wherein the pathological state is cancer.

62. (Withdrawn): The method of claim 61, wherein the cancer is pancreatic or breast cancer.

63. (Withdrawn): The method of claim 57, wherein the target nucleic acid sequence comprises some or all of a consecutive sequence of bases in an RNA transcript.

64. (Withdrawn): The method of claim 57, wherein the RNA transcript is produced from an oncogene or proto-oncogene.

65. (Withdrawn): The method of claim 57, wherein the targeting moiety is a protein, a glycoprotein, a peptide, a steroid, a carbohydrate, a lipid or a vitamin.

66. (Withdrawn): The method of claim 57, wherein the targeting moiety is IGF1, ST, or fragments or homologs thereof.

67. (Withdrawn): The method of claim 57, wherein the cells are contacted with the compound by an enteral or parenteral route of administration.

68. (Withdrawn): The method of claim 67, wherein the parenteral administration routes are selected from the group consisting of intravascular administration; peri- and intra-tissue injection; subcutaneous injection; subcutaneous deposition; subcutaneous infusion; and direct application to the tumor or to tissue surrounding a tumor.

69. (Previously Presented): A method of retaining a compound inside a cell, comprising:

(1) contacting a cell that contains transcripts comprising a target nucleic acid sequence with the compound of claim 1, such that the compound binds to the cell via the

targeting moiety and is internalized by the cell;

(2) allowing the PNA to bind to the target nucleic acid sequence and retain the compound inside the cell.

70. (Original): The method of claim 69, wherein the diagnostic moiety comprises a dendrimer.

71. (Original): The method of claim 69, wherein the target nucleic acid sequence comprises some or all of a consecutive sequence of bases in an RNA transcript.

72. (Original): The method of claim 71, wherein the RNA transcript is produced from an oncogene or proto-oncogene.

73. (Original): The method of claim 69, wherein the targeting moiety is a protein, a glycoprotein, a peptide, a steroid, a carbohydrate, a lipid or a vitamin.

74. (Withdrawn): The method of claim 69, wherein the targeting moiety is IGF1, ST, or fragments or homologs thereof.

75. (Original): The method of claim 69, wherein the cell is a cancer cell.

76. (Canceled)

77. (Canceled)

78. (Canceled)

79. (Canceled)

80. (Previously Presented): The method of claim 51, wherein the RNA transcript is heteronuclear RNA or messenger RNA.

81. (Canceled)

82. (Previously Presented): The method of claim 51, wherein the oncogene or proto-oncogene is selected from the group consisting of MYC, K-RAS, c-myb, bcr-abl, p53, CCND1, HER2, c-FMS, c-KIT, c-MET, c-TRK, c-NEU, c-SRC, c-FES, c-ABL, c-FGR, c-YES, c-ERBA, c-EVI-1, c-GLI-1, c-MAF, c-LYL-1, c-ETS, c-FOS, c-JUN, c-MYB, b-MYB, N-MYC, L-MYC, c-REL, c-VAV, c-SKI, and c-SPI.

83. (Original): A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.

84. (Canceled)

85. (Canceled)

86. (Original): A pharmaceutical composition comprising the compound of claim 4 and a pharmaceutically acceptable carrier.

87. (Withdrawn): A pharmaceutical composition comprising the compound of claim 5 and a pharmaceutically acceptable carrier.

88. (Currently Amended): A compound comprising a polymeric diagnostic moiety (X) covalently conjugated to at least one PNA (P) and at least one targeting moiety (T) that is capable of binding to a cell surface molecule, wherein the PNA comprises a base sequence that is complementary to a target nucleic acid sequence, or pharmaceutically acceptable salts thereof, provided that the compound is represented by a formula

X-L1-P-L2-T

or pharmaceutically acceptable salts thereof, wherein L1 and L2 represent ~~a chemical bond or~~ at least one linking moiety, L1 is covalently bound to X and P and L2 is covalently bound to P and

T, L1 and L2 can be the same or different, and are independently selected from the group consisting of -NH(O)C-CH2CH2-C(O)O- and -HN-CH2CH2-O-CH2CH2-O-CH2C(O)O, (Gly)4 and 4-amino butyric acid and wherein the polymeric diagnostic moiety (X) comprises at least one of a linear oligomeric polychelant, a branched oligomeric polychelant, a dendrimer, a bridged dendrimeric or polymeric moiety, a plurality of chelants optionally complexed to one or more diagnostic metal ions, a diagnostic metal ion suitable for use in PET imaging, a radioactive halogen, a plurality of linear, cyclic or branched polyamino-polycarboxylic acid chelants or their phosphorous oxyacid equivalents, or an ultrasound contrast agent.

89. (Previously Presented): A compound consisting essentially of

(i) a polymeric diagnostic or therapeutic moiety (X) covalently conjugated to at least one PNA (P) and at least one targeting moiety (T) that is capable of binding to a cell surface molecule, wherein the PNA comprises a base sequence that is complementary to a target nucleic acid sequence, or pharmaceutically acceptable salts thereof, provided that the compound is represented by a formula

X-L1-P-L2-T

or pharmaceutically acceptable salts thereof, wherein L1 and L2 represent at least one linking moiety, provided that L1 is covalently bound to X and P and L2 is covalently bound to P and T; and

(ii) optionally, a pharmaceutically acceptable carrier.

90. (Previously Presented): A diagnostic imaging method, comprising:

(1) contacting cells of a subject that contain transcripts comprising a target nucleic

acid sequence with a compound of claim 89 wherein X is the diagnostic moiety, such that the compound binds to the cells via the targeting moiety and is internalized by the cell;

(2) allowing the PNA to bind to the target nucleic acid sequence and retain the compound inside the cell; and

(3) detecting the compound within the cells.

91. (Previously Presented): A method of retaining a compound inside a cell, comprising:

(1) contacting a cell that contains transcripts comprising a target nucleic acid sequence with the compound of claim 89, such that the compound binds to the cell via the targeting moiety and is internalized by the cell;

(2) allowing the PNA to bind to the target nucleic acid sequence and retain the compound inside the cell.

92. (Previously Presented): A pharmaceutical composition comprising the compound of claim 89 wherein X is the diagnostic moiety and a pharmaceutically acceptable carrier.

93. (New): The compound of claim 1, wherein L1 and L2 can be the same or different, and further wherein the diagnostic or therapeutic moiety is separated from the PNA by a distance of from about 10A to about 30A by one or more spacer moieties.

94. (New): The compound of claim 88, wherein L1 and L2 can be the same or different, and further wherein the diagnostic or therapeutic moiety is separated from the PNA by a distance of from about 10A to about 30A by one or more spacer moieties.

95. (New): The compound of claim 89, wherein L1 and L2 can be the same or

different, and further wherein the diagnostic or therapeutic moiety is separated from the PNA by a distance of from about 10A to about 30A by one or more spacer moieties.

96. (New): The compound of claim 93, wherein L1 and L2 can be the same or different, and further wherein the spacer moiety is hydrophilic.

97. (New): The compound of claim 94, wherein L1 and L2 can be the same or different, and further wherein the spacer moiety is hydrophilic.

98. (New): The compound of claim 95, wherein L1 and L2 can be the same or different, and further wherein the spacer moiety is hydrophilic.

99. (New): The compound of claim 96, further comprising a branched dendrimer.

100. (New): The compound of claim 97, further comprising a branched dendrimer.

101. (New): The compound of claim 98, further comprising a branched dendrimer.